Adverse drug reaction reporting in a pharmacovigilance centre of Nepal

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RESEARCH

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Abstract

Background

Pharmacovigilance is the "science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems". Nepal joined the international pharmacovigilance programme as a full member in 2007. KIST Medical College, Lalitpur, Nepal joined the national programme as a regional centre from mid-July 2008. Currently, the pattern and scope of adverse drug reactions (ADRs) in Nepal remains unexplored.

Aims

To observe and analyse the pattern of ADRs at KIST Medical College, Lalitpur, Nepal.

Method

A retrospective analysis of all ADRs reported to the centre from mid July 2008 to July 2011 was performed. Data was analysed for ADR severity, causality, and preventability.

Results

A total of 113 ADR reports were obtained from various clinical departments. The maximum number of reactions was due to antimicrobials, followed by anti-hypertensives and NSAIDs.

Conclusion

Antimicrobials were the commonest group of drugs causing ADRs and the most commonly seen ADR was maculopapular rash followed by diarrhea and vomiting.

Key Words

Adverse drug reactions, Nepal, pharmacovigilance, spontaneous reporting

What this study adds:

- The study examines ADRs reported over a three-year period to a regional pharmacovigilance centre in Nepal
- The possible reasons for under-reporting are discussed in this study.
- The study highlights the need for further research to identify causes for under-reporting

Background

Pharmacovigilance is the "science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems".[1] Pharmacovigilance plays an important role in rational use of medicines by providing information about adverse drug reactions (ADRs) in the general population.[1] In the year 2004, pharmacovigilance activities were initiated in Nepal which became a full member of the international pharmacovigilance programme in 2007.[2] The Department of Drug Administration (DDA), the national drug regulatory authority of Nepal acts as the national centre for ADR monitoring. KIST Medical College joined the programme as a regional centre from July 2008.

Pharmacovigilance in Nepal: In Nepal, hospitals report ADRs to the regional pharmacovigilance centres from where reports are sent to the national pharmacovigilance centre. From there reports are sent to the Uppsala Monitoring Centre (UMC), Sweden, the international centre. At present, there are six regional pharmacovigilance centres located in teaching hospitals which report ADRs to the national centre via a web-based system called 'Vigiflow'.

In Nepal, there is no mandatory law necessitating drug manufacturers to submit safety data from the Nepalese population prior to approval of the medicines. Hence, it is very necessary to monitor side effects of the medicines

available in the market as the information collected during the pre-marketing phase is inevitably incomplete with regard to possible ADRs.[3] Nepal is a developing country and has several medicine use problems. The majority of drugs used are manufactured in foreign countries and the safety profile of the excipients, diluents, binders, stabilisers and other additives used to prepare medicines are not known. The genetic make-up of the Nepalese population is varied which might be a predisposing factor for ADRs.[4,5] The annual consumption of drugs in Nepal is estimated to be worth over 3719.3 million Nepalese rupees (US$53.12 million), with an estimated 28.5% increase in consumption every year.[6]

Method

The study was a retrospective analysis of ADRs reported from mid July 2008 to July 2011 to the regional pharmacovigilance centre at the KIST Medical College, Lalitpur, Nepal. The medical college has an attached 300-bed tertiary care hospital.

ADR reporting forms designed to report reactions to the centre were available in all wards and outpatient departments (OPDs) of the hospital. Patient and drug details, date of starting and stopping the drug and date of reporting the ADR, brief description of reaction, and name and signature of the reporter are requested in the ADR reporting form. The information regarding reaction and other basic information was completed and submitted to the Pharmacovigilance centre for analysis of the case. Technical assessments for causality, severity and preventability were performed. Naranjo algorithm was used to categorise ADRs for causality as possibly, probably or definitely for each drug.[7] Modified Hartwig and Siegel scale was used to categorise the reported ADRs into different levels as mild, moderate or severe.[8] Shumock and Thornton scale was used to determine the preventability of an ADR.[9]

Table 1: Common classes of drugs causing ADRs

Drug Class	Number (Percentage)
Antimicrobials	51 (45.13%)
Antihypertensives	15 (31.27%)
NSAIDs	13 (11.5%)
Proton pump inhibitors	5 (4.42%)
Corticosteroids	5 (4.42%)
Thiazides	5 (4.42%)
Anti-epileptics	5 (4.42%)
Bronchodilators	3 (2.65%)

Results

The total number of adverse drug reaction reports over the audit period was 113. More than half the ADRs reported occurred in female patients (55.35%), and nearly half (44.24%) the patients were in the age group of 21-40 years. Sixty-eight (60.17%) ADRs were reported by the Department of Medicine followed by the Paediatrics Department [18 (15.92%)]. Antimicrobials were the class of drugs causing the highest number of ADRs followed by antihypertensive drugs (Table 1).

Most common drugs causing ADRs were azithromycin, amlodipine, ciprofloxacin, diclofenac, fluconazole, ceftriaxone, amoxicillin, carbamazepine and thiazides.

Causality assessment as per Naranjo's scale showed that 60 (67.80%) ADRs were probably caused by the drug and 40 (45.50%) ADRs were possibly caused by the drug. The severity assessment showed that 12 (10.61%) ADRs were mild level (1), 54 (47.70%) ADRs were moderate level (2) 34 (30.08%) ADRs were moderate level (3) 8 (7.07%) reactions were moderate level 4(a) and 5 (4.42%) ADRs were moderate level 4(b).

Preventability assessment showed that only 13 (11.50%) of the reported ADRs were definitely preventable. Thirty (26.54%) ADRs were probably preventable and 70 (61.94%) were not preventable.

Table 2 shows the different types of adverse drug reactions reported along with their frequency.

Table 2: Types of adverse drug reactions reported

Reaction	Number (frequency)
Maculopapular rash	25 (22.12%)
Vomiting	19 (16.81%)
Diarrhea	13 (11.50%)
Rash	12 (10.61%)
Drug fever	4 (3.53%)
Pedal oedema	4 (3.53%)
Headache	2 (1.76%)
Vertigo	2 (1.76%)
Elevation of liver enzymes	2 (1.76%)
Bradycardia	2 (1.76%)
Tremor	2 (1.76%)
Dry cough	2 (1.76%)
Giddiness and dizziness	2 (1.76%)
Swelling of limbs	2 (1.76%)
Rigors and chills	2 (1.76%)

Discussion

There was a higher prevalence of ADRs in females with a female: male ratio of 1: 0.74, which is comparable with

other studies; one study showed a female: male ratio of 1: 0.87[10] while another study showed a ratio of 1.8:1.[11]

Females have been identified as being at higher risk for developing ADRs. The underlying reasons may be various physiological reasons like menstruation, menarche, pregnancy, lactation and menopause and a stronger immune response in women. In a study from a South Indian hospital, the majority of patients experiencing ADRs were in the age group 21-40 years.[10] Another study in a tertiary care centre in South India showed the age group 20-39 years suffered from more ADRs.[12]

The top 10 drugs responsible for causing ADRs reported to the national pharmacovigilance centre from centres all over the country were carbamazepine, phenytoin, amoxicillin, ciprofloxacin, diclofenac, isoniazid, ibuprofen, paracetamol, tramadol and cotrimoxazole.[13]

The skin is the largest organ of the body and most ADRs are seen in the skin.[14] Maculopapular rashes were the most commonly reported type of ADR. This result is in concordance with the studies by Sushma et al.[10] and Puavilai and colleagues.[15] In our study, azithromycin was the most common drug causing ADRs followed by ibuprofen and amlodipine. In a study done by Fiszensin-Albala and co-workers from France, the main drug group responsible for ADRs was antibiotics.[16] However, another study done by Noel and co-workers showed anti-epileptics as the major causative drugs for causing the ADRs.[17]

The current system of reporting ADRs remains in its infancy. Future plans for the development of this system include: strengthening the reporting system by training the new faculties and medical officers in each department about the pharmacovigilance programe in our hospital; following up all clinical departments weekly for improving the quality of reporting; providing feedback to the clinicians about the progress of their reported reactions to facilitate an improvement in the problem of under-reporting. Medication errors and error reporting are still controversial issues and will have to be discussed before an error reporting programme can be initiated.

Limitations

Our study did not evaluate the association of ethnic group, caste and religion, and polypharmacy with ADRs. Also, some of the reports for ayurvedic and complementary medicines could not be assessed due to the lack of information regarding its composition, dose and frequency. Lack of awareness and information about medication errors and also non-availability of medication error reporting systems which is an important part of pharmacovigilance is a major limitation.

Conclusion

Antimicrobials were the commonest group of drugs causing ADRs and the most commonly observed ADR was maculopapular rash followed by vomiting and diarrhoea. Efforts are underway to encourage clinicians, nurses and other allied healthcare workers to report all ADRs even suspected ones, with the aim of improving medicine use.

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CONFLICTS OF INTEREST

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